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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/925,065	08/08/2001	David G. Wang	108827.135	2603
23483	7590	02/18/2005	EXAMINER	
WILMER CUTLER PICKERING HALE AND DORR LLP 60 STATE STREET BOSTON, MA 02109			SWITZER, JULIET CAROLINE	
			ART UNIT	PAPER NUMBER
			1634	
DATE MAILED: 02/18/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/925,065

Applicant(s)

WANG, DAVID G.

Examiner

Juliet C. Switzer

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of SEQ ID NO: 1 in the reply filed on 10/4/04 is acknowledged. The traversal is on the ground(s) that it would not be an undue burden to search all of the sequences in this application since all 12,108 sequences were provided to the office in computer form. This is not found persuasive because regardless of the form that the sequences were provided, the search and examination of the over 12,000 nucleotide sequences would indeed be an undue burden on the examiner. First, the search burden on computer resources itself would be enormous requiring over 60,000 hours of computer time to run the searches. Each search provides extensive output which would then have to be reviewed by the examiner, which is also a substantial time commitment. Each search output would take a minimum of one hour to carefully review by the examiner, for a total then, of at least 12,108 hours of examiner time. Further, due to the nature of the claimed invention, and the fact that many of these sequences are fragments of known human genes, separate literature searches would be required for each sequence to determine if the polymorphisms were disclosed in a journal reference, for example, but not entered into a computer database. Further, searches would have to be conducted to determine if the claimed inventions are supported by a well established utility in the prior art. The search effort to examine even a single nucleotide sequence is significant, for multiple sequences it is an undue burden, contrary to applicant's assertion.

The requirement is still deemed proper and is therefore made FINAL.

Specification/ Compact Disc Submission/Sequence Listing

2. The specification is objected to because it refers to "Figure 2" and then describes a detailed table. However, there is no such table in the figures or in the specification. Newly filed drawings on 3/11/02 include only a single drawing sheet marked as 1/1. Clarification is required. It appears that perhaps a portion of this application (the table in question) is contained on a compact disc (see originally filed figure 2 which is a photocopy of compact disks. If that is the case, then the application is not in proper form (see below).

3. Portions of this application are contained on compact disc(s). When portions of an application are contained on a compact disc, the paper portion of the specification must identify the compact disc(s) and list the files including name, file size, and creation date on each of the compact discs. See 37 CFR 1.52(e). Compact disc(s) containing Figure 2 or a table as described in the description of figure 2 as well as a compact disc containing the paper copy of the sequence listing are not identified in the paper portion of the specification with a listing of all of the files contained on the discs. Applicant is required to amend the specification to identify each disc and the files contained on each disc including the file name, file size, and file creation date.

4. This application contains compact disc(s) as part of the originally filed subject matter, but does not contain an incorporation by reference statement for the compact discs. See 37 CFR 1.77(b)(4). Applicant(s) are required to insert in the specification an incorporation-by-reference of the material on the compact disc(s).

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (5474796).

The instant claim is drawn to a probe consisting of an oligonucleotide that is complementary to a SNP nucleic acid shown in SEQ ID NO: 1. The claim is interpreted as including any probe which is complementary over its entire length to any portion of SEQ ID NO: 1. The claim does not require that the probe be complementary to any particular portion of SEQ ID NO: 1, nor that the probe be complementary to SEQ ID NO: 1 in its entirety. Further, even if the claim did require that the probe overlap with a particular portion of SEQ ID NO: 1, it sets forth no requirement for any particular allele of the polymorphic position at 205 of SEQ ID NO: 1 to be present, and the ambiguous code used in the sequence listing includes two possible alleles.

Brennan teaches an array having thereupon every possible permutation of the 10-mer oligonucleotide. The oligonucleotides are spaced as 7 nm intervals (Col. 9, Example 4, lines 49-55). Thus, each oligonucleotide is an isolated spot on the array. In this way, Brennan teaches every possible oligonucleotide consisting of 10 successive nucleotides of the complement of SEQ ID NO: 1. Included within this set would be many oligonucleotides that are complementary to SEQ ID NO: 1, including some which would overlap with and contain the polymorphic position within SEQ ID NO: 1 located at position 205 of SEQ ID NO: 1. Thus, the teachings of Brennan anticipate the claimed invention.

Claim Rejections - 35 USC § 103

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7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Otterness et al. (Clin. Pharmacol. Ther, 1997; 62:60-73) in view of GenBank AB045146 (GI: 8777468, 22 August 2000).

The instant claim is drawn to a probe consisting of an oligonucleotide that is complementary to a SNP nucleic acid shown in SEQ ID NO: 1. Instant SEQ ID NO: 1 is a fragment from within intron 9 of the thiopurine s-methyltransferase gene. The claim is interpreted as including any probe which is complementary over its entire length to any portion of SEQ ID NO: 1. The claim does not require that the probe be complementary to any particular portion of SEQ ID NO: 1, nor that the probe be complementary to SEQ ID NO: 1 in its entirety. Further, even if the claim did require that the probe overlap with a particular portion of SEQ ID NO: 1, it sets forth no requirement for any particular allele of the polymorphic position at 205 of SEQ ID NO: 1 to be present, and the ambiguous code used in the sequence listing includes two possible alleles.

Otterness et al. teach methods for discovery of polymorphisms within the human TPMT gene, and in particular, teach the use of fragments from within introns for the amplification of exons, as well as for the amplification of portions of introns for polymorphism discovery (see, for example, Table 1). These sequences consist of fragments of the introns of the TPMT gene.

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Otterness et al. do not teach a fragment which consists of an oligonucleotide complementary to any portion of SEQ ID NO: 1.

The GenBank record provides the entire nucleotide sequence of the genomic DNA encoding human TPMT. Instant SEQ ID NO: 1 consists of nucleotides 24098-24532 of this sequence. At position 205 of instant SEQ ID NO: 1 there is an "r" which is the IUPAC symbol for either A or G. The GenBank record has an A at this position.


It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have produced additional primers that are within the introns of the TPMT gene using the sequence taught by Otterness et al., including fragments of intron IX of the gene. One would have been motivated to produce these fragments for amplification and detection of both the exons and introns of the gene for further polymorphism discovery, since Otterness et al. exemplify that the introns of this gene contain polymorphisms (p. 69, 2nd column) and because Otterness et al. teach it will ultimately be necessary to completely understand mechanisms involved in the regulation of TPMT activity in humans to individualize thiopurine therapy (p. 71, 2nd column). Part of this understanding would be study of potential regulatory regions within introns of the gene, for example to screen for additional polymorphisms. The production of additional primers and probes from within the intron regions would be useful to this end. Therefore, the broadly claimed invention is prima facie obvious in view of the prior art.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday through Wednesday, from 9:00 AM until 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor,

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W. Gary Jones can be reached by calling (571) 272-0745. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.


Juliet C. Switzer
Primary Examiner
Art Unit 1634

February 17, 2005